cytometric analysis after 24 hours in culture unless otherwise indicated. This enhanced cell recovery because monocytes, which initially adhere to plastic vessels transiently detach from culture wells at 24-48 hours.

In the Claims:

Please cancel claims 5-10 without prejudice.

REMARKS

Claims 1-10 are pending in this application. Claims 5-10 were subject to a Restriction Requirement and have been withdrawn from consideration. Claims 1-4 have been rejected. Claims 5-10 have been canceled. The specification has been amended to correct typographical errors. Reconsideration is respectfully requested in light of the following remarks.

I. Restriction Requirement

The Restriction Requirement wherein Applicants elected with traverse Group I, claims 1-4, has been deemed proper and made final. Accordingly, Applicants have canceled claims 5-10 without

prejudice, reserving the right to file continuing applications on the canceled subject matter.

II. Objection to the Specification

The disclosure was objected to because of an informality. The Examiner suggests that at page 13, line 3, Table 1 is referred to but that Table I is not found in the specification as filed. Applicants have amended the specification to remove the term Table 1 and have instead inserted the name of a mediator tested. Withdrawal of this objection is therefore respectfully requested.

III. Rejection of Claims Under 35 U.S.C. 112, First Paragraph

Claim 2 has been rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Specifically, the Examiner suggests that the specification does not disclose a repeatable process to obtain the antibodies cited in the claim (MAC2-158, MAC2-48 and RM3/1). The antibodies are commercially available from Maine Biotechnology (http:/www.MainBiotechnology.

com/catalog/mainebio.cgi). It is therefore respectfully requested that this rejection be withdrawn.

IV. Rejection of Claims Under 35 U.S.C. 103(a)

Claims 1-4 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Coligan et al. (1991), in view of U.S. Patent 5,077,216 and Zwadlo et al. (1987), and the known fact disclosed at page 4, paragraph 1 of the specification as filed. The Examiner suggests it would have been *prima facie* obvious for one of ordinary skill in the art to substitute the antibodies taught by the '216 patent and Zwadlo et al. in the ELISA assay taught by Coligan et al. to detect and monitor the presence of CD163 in a sample such as human plasma during an inflammatory condition because ELISA assays are known to be very sensitive and useful for screening biological fluids as taught by Coligan et al. and monitoring the course of inflammatory conditions by detecting CD163 is important as taught by Zwadlo et al. Applicants respectfully traverse this rejection.

Applicants acknowledge that at page 4, paragraph 1, it is taught in the specification that p155 and CD163 are the same entity.

Coligan et al. (1991) is a book chapter that describes the ELISA assay method in general terms. Although the use of this assay is described, nowhere does this reference teach or suggest antibodies directed against CD163 or use of ELISA to detect the presence of CD163 in any sample type or use of an ELISA assay to monitor the course of an inflammatory condition.

U.S. Patent 5,077,216 discloses monoclonal antibodies that are capable of detecting p155, a human mononuclear phagocyte-specific antigen. Mac2-158 and Mac2-48 are disclosed. However, nowhere does this patent teach or suggest use of ELISA to detect the presence of CD163 in any sample type or use of an ELISA assay to monitor the course of an inflammatory condition.

Zwadlo et al. (1987) discloses a monoclonal antibody RM3/1 that detects a surface antigen on 20% of freshly isolated PBMCs and that this RM3/1 antigen is expressed late in the inflammatory process, during the healing phase. However, nowhere does this paper teach or suggest use of RM3/1 in an ELISA assay to detect the presence of CD163 in any sample type or use of an ELISA assay to monitor the course of an inflammatory condition.

To establish a *prima facie* case of obviousness, three basic criteria must be met. MPEP 2143. First, there must be some suggestion or motivation, either in the references themselves or

in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art must teach or suggest all claim limitations. In the case of the instant claims, although the antibodies were taught in the art and use of ELISA as a technique for antigen detection was known, nowhere in the references cited do the authors teach or suggest that these teachings could be combined to result in the claimed method. There is no suggestion or motivation in the references cited to combine the teachings of these references as required under MPEP 2143.01. Further, one of skill would not have been motivated to combine the references cited since it is only with the teachings of the specification in hand that CD163 is shown to be successfully detected in biological samples at sensitivity high enough to allow for monitoring of the course of an inflammatory condition, again as only known after reading the teaching of the specification as filed. MPEP 2143 requires that an expectation of success be provide by the cited references alone, not in light of the teachings of the instant invention. Finally, as stated in MPEP 2143.01, the fact that references can be combined is not

sufficient to establish *prima facie* obviousness. Accordingly, withdrawal of this rejection is respectfully requested.

V. Conclusion

Applicants believe that the foregoing comprises a full and complete response to the Office Action of record. Accordingly, favorable reconsideration and subsequent allowance of the pending claims is earnestly solicited.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "**VERSION WITH MARKINGS TO SHOW CHANGES MADE**."

Respectfully submitted,

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Date: **May 23, 2002**

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Specification:

At page 4, lines 14-30, the paragraph has been replaced with the following rewritten paragraph:

--Previous studies using mAbs RM3/1, Ber-Mac3 and others have reported that only 0%-40% of circulating monocytes are positive for CD163 (Hogger, P. et al. 1998. *Pharm Res*. 15:296-302; Hogger et al. 1998. *J. Immunol*. 161:1883-1890; Zwadlo, G. et al. 1987. *Exp. Cell Biol*. 55:295-304; Backe, E. et al. 1991. *J. Clin. Path*. 44:~~946-953~~ 936-945; van den Heuvel, M. et al. 1999. *J. Leuk. Biol*. 66:858-866). However, previous studies with another antibody to p155, a molecule that has been shown to be identical to CD163, Mac 2-48, has consistently demonstrated that virtually all freshly isolated monocytes are positive for CD163. To address the possibility that sub-optimal detection of the lower affinity RM3/1 and Ber-Mac3 antibodies (previously used only with FITC labeled secondary antibodies) might account for this discrepancy, freshly isolated PBMCs were stained with FITC conjugated AML 2.23 (anti-CD14) and biotinylated RM3/1 or biotinylated Mac2-48, followed by detection with SAPE.--

At page 8, lines 33-35 and page 9, lines 1-9, the paragraph has been replaced with the following rewritten paragraph:

--The dose response curve for the IL-10 effect on CD163 expression demonstrates a dynamic range of IL-10 concentrations that is from 0.1 ng/ml to 10 ng/ml. This is consistent with previous findings concerning the effect of IL-10 on a wide range of monocyte functions such as tissue factor expression and associated procoagulant activity (Ernofsson, M. et al. 1996. *Br. J. Haematol.* 95:249-257; ~~Ones~~ Osnes, L.T. et al. 1996. *Cytokine* 8:822-827), as well as MIP-1α (Berkman, N. et al. 1995. *J. Immunol.* 155:4412-4418), metalloproteinase (Lacraz, S. et al. 1992. *J. Clin. Invest.* 90:382-388) and TNF receptor (Hart, P.H. et al. 1996. *J. Immunol.* 157:3672-3680) expression.--

At page 12, lines 32-33 and page 13, lines 1-7, the paragraph has been replaced with the following rewritten paragraph:

--For cytokine treatment studies, isolated PBMCs were suspended in hepes buffered RPMI 1640/0.05% gentamicin/10% FBS at a concentration of 2.0 x 10^6 to 2.5 x 10^6 cells/ml and cultured in 96 well plates at 37°C and 5% CO_2 in the presence of various

mediators ~~(Table 1)~~ such as IL-10. Mononuclear cells were stained for flow cytometric analysis after 24 hours in culture unless otherwise indicated. This enhanced cell recovery because monocytes, which initially adhere to plastic vessels transiently detach from culture wells at 24-48 hours.--

In the Claims:

Claims 5-10 have been canceled without prejudice.